Case Report

Misdiagnosis of Wilson's Disease in a Patient with Psychiatric Symptoms

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ABSTRACT

Therapeutic outcome of Wilson's disease significantly depends upon its early recognition. As Wilson's disease is a rare disorder with protean manifestations, its diagnosis and subsequent treatment are often delayed. We elaborate here the case of a young boy who had initially presented with psychiatrc symptoms suggestive of dissociative fugue followed by withdrawn behaviour and was treated by a psychiatrist with minimal response. This was associated with symptoms of tremors, hypersalivation, and slowness of movements. This case highlights the delay in diagnosing Wilson's disease when faced with the case of a young adult with psychiatric manifestations. It is extremely important for physicians, psychiatrists and health professionals at primary care level to recognize and diagnose this treatable disease at an early stage.

Key words: *Misdiagnosis, psychiatric illness, Wilson's disease*

INTRODUCTION

Wilson's disease (WD) is an autosomal recessive disease, involving a defect of copper transport by hepatic lysosomes, caused by mutations in the ATP7B gene that lies on chromosome 13q14.3. Reduced biliary excretion of copper results in a net positive copper balance and copper deposition in the liver, brain, kidneys, and skeletal system.[1] WD is one of the few curable disorders provided; it is diagnosed and treated early. Misdiagnosis is common; the disease is rare and has protean clinical manifestations. We report a young man presenting with extrapyramidal signs and mutism, who was initially treated as a psychiatric disorder.

Access this article online	
Website: www.ijpm.info	**Quick Response Code**
DOI: 10.4103/0253-7176.185949	

CASE REPORT

A young male presented with the chief complaints of withdrawn behavior, decreased verbal output, and decreased self-care for the last 9 months followed by tremulousness, increased salivation, and slowness of activities for the last 6 months. Detailed history revealed a gradual onset of withdrawn behavior. He would not be affected emotionally by the events taking place in the household, as opposed to his usual self. He would not participate in the household activities and would do anything only on the insistence of his family members. Previously, he used to work in the fields and feed the

How to cite this article: Nimisha D, Dhruv B, Vikas M, Sneh JK, Rakesh S. Misdiagnosis of Wilson's disease in a patient with psychiatric symptoms. Indian J Psychol Med 2016;38:353-6.

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animals, but, after the onset of the illness, gradually he stopped doing these things and would stay at home most of the time. At the start of the illness, he would initiate conversation at times, but, over a month, his interaction reduced so much that he would reply only when spoken to. At times, he would wander in the fields but would come back home. He had also stopped spending time with his friends. Occasionally, once in 5-6 days, he would be seen smiling to self, but when asked about it, he would deny any such thing. Over a period of 3 months, he had stopped taking a bath regularly and often would not even change his clothes when not insisted. He was shown to several faith healers during the course of the initial 3 months, but there was no improvement in his condition. After about 3 months into the illness, there was a discrete episode of the patient wandering away from his house at night. He was found in the morning and did not recall any of the events at night and simply said that he had reached the place in the morning itself. Following that incident, the patient stopped taking food himself and had to be fed by the mother. He remained withdrawn and apathetic and was unable to carry out the activities of daily living. He was shown to a psychiatrist, and the treatment was started with antipsychotics. Initially, tablet Risperidone 2 mg BD was given and was subsequently replaced by tablet Olanzapine 10 mg HS when no response was obtained in 2 weeks. Later, tablet amisulpride 200 mg HS was added. About 4 months from the start of the illness and after about a week of starting medications, the parents also noticed that the patient had developed tremulousness of both hands which was interfering with the day-to-day activities. It was also noticed that the salivation had increased and over a period of 3 weeks, drooling of saliva from the mouth was noticed. Gradual slowness of movements was also observed. There was not much improvement in the condition of the patient. The patient was then taken to a neurologist 2 months later, and medications were started, the records of which are unavailable. He was then brought to neurology out-patient department for consultation. The patient was born of a nonconsanguineous marriage and had two siblings. There was no history of jaundice in the patient or his siblings.

On general physical examination, the patient had a dystonic facies with a vacuous smile and pooling of saliva in the mouth. On neurological examination, higher mental function examination was not possible as the patient was mute. However, comprehension was intact as the patient was following commands such as being asked to raise his respective hand. On gait examination, the patient had short stepping gait with decreased arm swing. Motor examination revealed bilaterally symmetrical rigidity with dystonic finger posturing and striatal toe with postural tremors. Ophthalmological examination revealed presence of Kayser-Fleischer (KF) ring.

Laboratory investigations revealed markedly decreased serum ceruloplasmin (3 mg/dl; normal range 15-45 mg/dl) and markedly elevated 24 h urinary copper (262.02 μg/day; normal range 15-60 μg/day). The rest of the hematological and biochemical investigations were normal.

Magnetic resonance imaging brain revealed signal intensity alterations in bilateral basal ganglia [Figure 1] and thalami [Figure 2]. Gradient-recalled echo sequence showed blooming in bilateral basal ganglia [Figure 3]. Overall findings were suggestive of WD [Figure 1]. The parents and siblings were also examined and did not show a KF ring; serum ceruloplasmin was also normal.

The patient was started on tablet D-penicillamine 100 mg BD.

DISCUSSION

Our patient presented with mutism, a vacuous smile, parkinsonian features, dystonic finger posturing, and bilateral striatal toes. Bedside, examination revealed a brownish pigmentation in the upper part of the cornea, which was confirmed to be KF ring on slit lamp examination, and had a low serum ceruloplasmin with increased urinary copper excretion. He was, however, misdiagnosed to be suffering from a psychiatric disorder at the initial consultation with a psychiatrist and prescribed neuroleptic drugs. A correct diagnosis of WD was made, after a delay of 9 months, when he came for consultation to us.

In a consecutive series of 307 patients seen over a period of 30 years in a tertiary care hospital, diagnostic errors by referring doctors were seen in 192 (62.5%). It is noteworthy that 37 patients were misdiagnosed during the first evaluation even in the tertiary care hospital.[2] Walshe and Yealland reported a mean delay in diagnosis

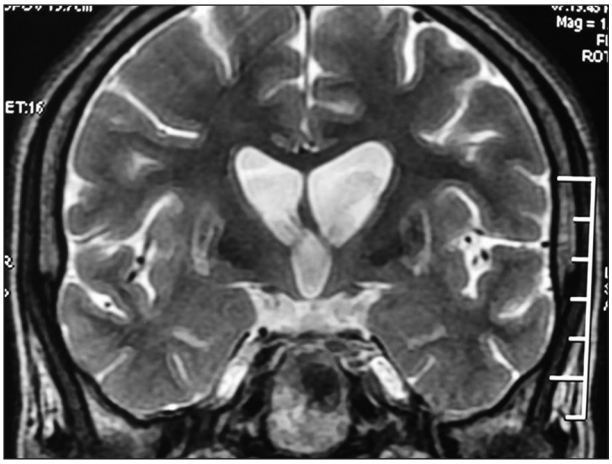

Figure 1: Coronal T2-weighted image showing hyperintense lesions in bilateral basal ganglia

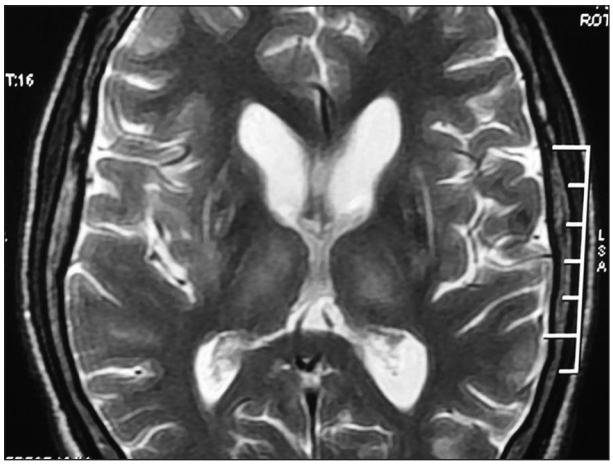

Figure 2: Bilateral thalamic hyperintensities seen on a T2-weighted image

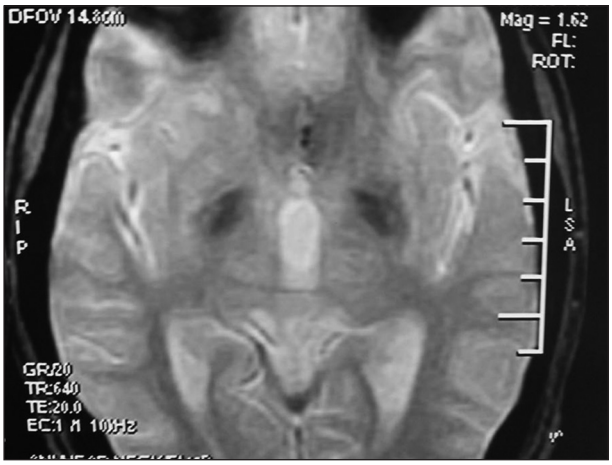

Figure 3: Gradient recalled echo images showing blooming effect in bilateral basal ganglia

of 12.8 months.[3] Incorrect diagnoses were as diverse as flat feet, myxedema, myasthenia gravis, encephalitis, multiple sclerosis, Parkinson's disease, schizophrenia, depression, anxiety state, etc. Hu *et al.* noted that among 1011 cases of hepatolenticular degeneration, 516 cases were initially misdiagnosed, 193 cases failed to be diagnosed as a specific disease, and only 302 cases were correctly diagnosed within 3 months after the onset. The curative effect was better in the group with early diagnosis than in the groups with misdiagnosis and without a precise diagnosis ($P < 0.01$).[4]

It has been reported that early manifestations of WD are generally hepatic or neurological (40% each) while the remainder present with psychiatric, hematological, renal, or osteochondrotic symptoms.[5] Walshe and Yealland analyzed the initial diagnosis of 136 patients with WD and observed that it fell into four groups, that is, organic disorder other than WD 25.7%, psychiatric illness 23.5%, seizure disorder 19.1%, and WD 31.6%.[3] Psychiatric symptoms are often the first manifestation of the disease and can obscure the diagnosis. There are several neuropsychiatric symptom clusters established for WD patients: Personality disorders, mood disorders, cognitive deficits, psychotic manifestations, etc.[6] Psychiatric symptoms can occur before, concurrent with or after the diagnosis and treatment for WD. In the brain, copper is commonly deposited in the basal ganglia, particularly in the putamen and globus pallidus.[5] Damage to these areas leads to the neuropsychiatric symptoms seen in WD. According to a recent review, 30-40% of patients have psychiatric manifestations at the time of diagnosis, and about 20% have already seen a psychiatrist prior to the diagnosis of WD.[6,7]

The causes for delay in diagnosis are varied and include rarity of the disease, protean clinical manifestations, lack of awareness among treating physicians, laboratory errors in the estimation of copper and ceruloplasmin concentrations and evaluation for KF rings by an inexperienced ophthalmologist. The patients presenting with behavioral problems often receive antipsychotic agents. With the evolution of extrapyramidal symptoms, they are diagnosed as having a drug-related adverse event, although these are the hallmark of neurological WD.

In our case, the cause of the delay in diagnosis was mainly the predominant psychiatric presentation in the patient and also the delay in seeking help from proper health professionals. Furthermore, the development of extrapyramidal symptoms in the patient further complicated the case as its occurrence after taking medications could be due to medications itself that are drug-induced Parkinsonism as well as could have been an independent neurological symptom of WD.

This delay could have been prevented, had a proper neurological examination been done at the first referral, and laboratory investigations conducted early.

We believe that diagnostic possibility of WD should be considered in all young patients presenting with recent onset behavioral and personality changes. Screening tests for all suspected patients should include slit lamp examination for KF ring by an experienced ophthalmologist, abdominal ultrasound for architectural changes in liver, serum copper and ceruloplasmin, and 24 h urinary copper from a reliable laboratory.[8] The diagnosis of WD is not difficult if the clinician thinks of it and includes it in his differential diagnosis. However, it needs to be emphasized that there is no typical clinical picture and even in the same family, the presentation may be different.

Financial support and sponsorship
Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Brewer GJ, Yuzbasiyan-Gurkan V. Wilson disease. Medicine (Baltimore) 1992;71:139-64.
2. Prashanth LK, Taly AB, Sinha S, Arunodaya GR, Swamy HS. Wilson's disease: Diagnostic errors and clinical implications. J Neurol Neurosurg Psychiatry 2004;75:907-9.
3. Walshe JM, Yealland M. Wilson's disease: The problem of delayed diagnosis. J Neurol Neurosurg Psychiatry 1992;55:692-6.
4. Hu J, Lü D, Wang G. Study on the clinical misdiagnosis of hepatolenticular degeneration. Zhonghua Yi Xue Za Zhi 2001;81:642-4.
5. Scheinberg IH, Sternlieb I, editors. Wilson's disease. In: Major Problems in Internal Medicine. Philadelphia: W. B. Saunders; 1984. p. 23.
6. Akil M, Brewer GJ. Psychiatric and behavioral abnormalities in Wilson's disease. Adv Neurol 1995;65:171-8.
7. Zimbrean PC, Schilsky ML. Psychiatric aspects of Wilson disease: A review. Gen Hosp Psychiatry 2014;36:53-62.
8. Brewer GJ. Wilson's disease. In: Frucht SJ, Fahn S, editors. Movement Disorder Emergencies: Diagnosis and Treatment. Totowa, New Jersey: Humana Press; 2007. p. 195-208.